

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

- 1.-4. (Canceled).
5. (Previously presented) *Actinosynnema pretiosum* strain PF4-4 having ATCC accession number PTA-3921.
6. (Currently amended) An enhanced *Actinosynnema pretiosum* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~
7. (Currently amended) The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~
8. (Currently amended) The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~
9. (Currently amended) The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold

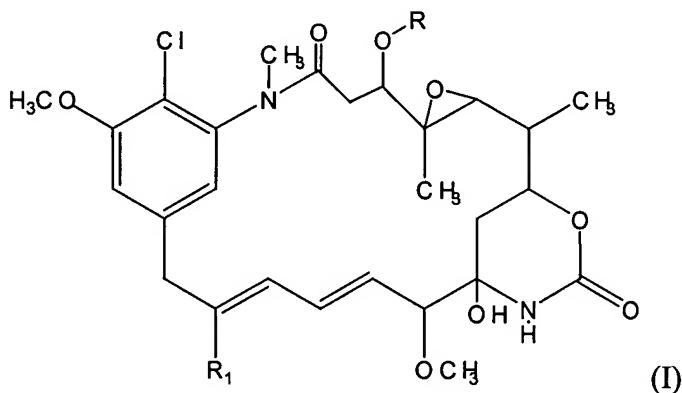
and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565) a parental strain from which the enhanced strain was derived.

10. (Canceled).

11. (Previously presented) The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the ansamitocin is ansamitocin P-3.

12. (Withdrawn) A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema pretiosum* strain of claim 6 in a culture medium comprising a suitable carbon source.

13. (Withdrawn) The method of claim 12, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R<sub>1</sub> is selected from the group consisting of methyl and hydroxymethyl.

14. (Withdrawn) The method of claim 13, wherein R is isobutyryl and R<sub>1</sub> is methyl.

15. (Withdrawn) The method of claim 12, wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

16. (Currently amended) An enhanced *Actinosynnema* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~

17. (Currently amended) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~

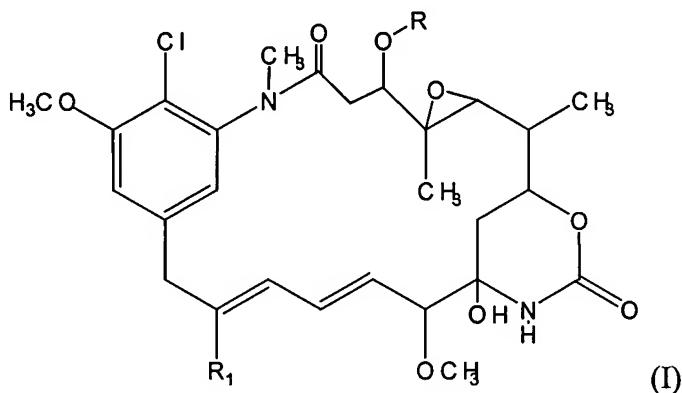
18. (Currently amended) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~a parental strain from which the enhanced strain was derived.~~

19. (Currently amended) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565)~~by a parental strain from which the enhanced strain was derived.~~

20. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the ansamitocin is ansamitocin P-3.

21. (Withdrawn) A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema* strain of claim 16 in a culture medium comprising a suitable carbon source.

22. (Withdrawn) The method of claim 21, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R<sub>1</sub> is selected from the group consisting of methyl and hydroxymethyl.

23. (Withdrawn) The method of claim 22, wherein R is isobutyryl and R<sub>1</sub> is methyl.

24. (Withdrawn) The method of claim 21, wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

25.-33. (Canceled).

34. (Currently amended) A method of producing an enhanced *Actinosynnema* bacterial strain that produces an ansamitocin in an amount of between about 1.2-fold and about

10-fold more than the amount produced by a parental *Actinosynnema* strain from which the enhanced strain ~~is was~~-derived, said method comprising:

- (a) treating a bacterial culture of an *Actinosynnema* strain ~~a bacteria that produces an ansamitocin~~ with a mutagen,
- (b) growing the treated bacteria of (a) under selective pressure,
- (c) selecting for an isolate of the product of (b) that exhibits increased production of an ansamitocin compared with the culture used in (a), and
- (d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than the culture used in (a) is obtained.

35. (Canceled).

36. (Currently amended) The method of claim 34, wherein said *Actinosynnema* ~~bacterial~~-strain is a strain of an *Actinosynnema pretiosum*.

37. (Withdrawn) The method of claim 34, wherein the mutagen is UV light or 1-methyl-3-nitro-1-nitroso-guanidine.

38. (Currently amended) The method of claim 34, wherein the enhanced *Actinosynnema* ~~bacterial~~-strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

39. (Currently amended) The method of claim 34, wherein the enhanced *Actinosynnema* ~~bacterial~~-strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

40. (Currently amended) The method of claim 34, wherein the enhanced *Actinosynnema* bacterial strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

41. (Withdrawn) The method of claim 34, wherein the selective pressure comprises growth of the treated bacteria on CM4-1 media.

42.-49. (Canceled).